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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/788,625	02/26/2004	Naoya Tsurushita	149 US UT01	6526

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PDL BIOPHARMA, INC.
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EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
05/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/788,625	TSURUSHITA ET AL.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/20/06 and 1/30/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-35* is/are pending in the application.

4a) Of the above claim(s) *34 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-29 are canceled.

Claims 30 and 33 have been amended.

Claims 34-35 have been added.

2. Newly added claims 34-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claims 30-33 are under consideration.

Objections/Rejections Withdrawn

4. The objection to the disclosure (i.e., Figure 1(B)) as containing a sequence that is encompassed by the sequences rules and requiring a sequence identifier is withdrawn in view of applicants' newly submitted sequence listing and the amendment to the Description of the Drawings filed 12/20/2006.

5. The objection to the Description of the Drawings because Figures 25 and 26 contain parts A-O and A-B, respectively that are not described in the Description of the Drawings is withdrawn in view of the amendments to the Description of the Drawings filed 12/20/2006.

6. The objection to the tile as not being sufficiently descriptive of the invention to which the claims are directed is withdrawn in view of the newly submitted title filed 12/20/2006.

7. The rejection of claims 30-33 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "expression vectors comprising DNA segments encoding a heavy chain variable region of a humanized chicken immunoglobulin..." or "expression vectors comprising...DNA segments encoding a light chain variable region of the humanized chicken immunoglobulin..." in claim 30 is withdrawn in view of the amendments to the claims.

8. The rejection of claim 33 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation "position selected from the group consisting of H67, H78, H93,

L46, L66 and L67 of the human acceptor immunoglobulin framework" is withdrawn in view of the amendment to the claim.

Response to Arguments

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. The rejection of claim 32 under 35 U.S.C. 112, second paragraph, for insufficient antecedent basis for the limitation "the amino acid of the human acceptor immunoglobulin framework..." is maintained.

The response filed 12/28/2006 states that the claim refers to replacing an amino acid of a human acceptor immunoglobulin framework when the replaced amino acid is rare for human immunoglobulin sequences at its. Applicant refers to the specification for the definition of the term "rare" and concludes that no issue of indefiniteness exists. This has been fully considered but is not found persuasive. Contrary to applicants' arguments the claim recites "the amino acid of the human acceptor framework" and not replacing *an amino acid* when the amino acid is rare for human immunoglobulin sequences at its position. Base claim 30 recites heavy chain frameworks from a human acceptor immunoglobulin and light chain frameworks from a human acceptor immunoglobulin, each chain comprising multiple framework amino acids. Thus, it remains ambiguous (i) which chain is being referenced (i.e., heavy or light chain) and (ii) which amino acid in the heavy or light chain is being referenced. What amino acid in the heavy or light chain human acceptor immunoglobulin frameworks is being referenced by the limitation "the amino acid of the human acceptor immunoglobulin framework"? See MPEP 2173.05(e).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. The rejection of claims 30-33 under 35 U.S.C. 103(a) as being unpatentable over Andris-Widhopf et al (Journal of Immunological Methods, 242:159-181, 2000) and Queen et al (U.S. Patent 5,530,101, issued 6/25/1996, IDS reference A1 filed 1/10/05) is maintained.

The response filed 12/20/2006 states that the claims as presently amended recite methods of producing a humanized chicken immunoglobulin wherein L1 and L2 of the light chain variable region frameworks from the human acceptor immunoglobulin are added to L1 and L2 of the humanized chicken immunoglobulin and L39A of the donor

chicken immunoglobulin is deleted in the humanized chicken immunoglobulin, wherein the amino acid numbering is according to Kabat. Applicant argues that there is nothing in the cited references that would have impelled the artisan to produce a humanized chicken immunoglobulin wherein L1 and L2 of the light chain variable region frameworks from the human acceptor immunoglobulin are added to L1 and L2 of the humanized chicken immunoglobulin and L39A of the donor chicken immunoglobulin is deleted in the humanized chicken immunoglobulin, wherein the amino acid numbering is according to Kabat. Applicant states that chicken is more evolutionary distant from human than mouse, so that the difference between chicken and human V genes in amino acid sequence and three dimensional structure is expected to be much larger than that between mouse and human V genes. Secondly, chicken light chain V genes, compared to mouse and human light chain V genes, carry two amino acid deletions, L1 and L2, at the N-terminus of mature proteins and one amino acid insertion at L39A in the framework 2. Applicants' arguments have been fully considered but are not found persuasive. In response to applicant's argument that there is nothing in the cited references that would have impelled the artisan to produce a humanized chicken immunoglobulin wherein L1 and L2 of the light chain variable region frameworks from the human acceptor immunoglobulin are added to L1 and L2 of the humanized chicken immunoglobulin and L39A of the donor chicken immunoglobulin is deleted in the humanized chicken immunoglobulin, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). As set forth in the previous Office Action, one of ordinary skill in the art at the time the invention was made would have been motivated and had a reasonable expectation of success to modify the chimeric chicken immunoglobulin of Andris-Widhopf et al and produce a humanized chicken immunoglobulin according to the method of Queen et al because chickens generate an immune response to highly conserved mammalian antigens that do not otherwise give rise to antibodies in mice and rabbits due to immunotolerance and thus, provide a useful source of clinically relevant antibodies that have human

therapeutic potential and the use of single VH and VL genes in chicken immunoglobulins simplifies the use of genetic techniques for antibody engineering as only one set of oligonucleotide primers is needed for each antibody chain and humanized chicken immunoglobulins would overcome the immunogenicity problem that remains with chimeric antibodies. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Semaker*, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983). The fact that applicant has recognized that unlike human immunoglobulins, no amino acid residues exist at positions L1 and L2 (Kabat numbering) of a chicken immunoglobulin and that chicken immunoglobulins also contain an extra amino acid residue between positions L39 and L40 (Kabat numbering), designated as L39A (e.g., see pg. 23 of the specification), does not render the claimed invention nonobvious, because the humanized chicken immunoglobulin as set forth in the teachings of Andris-Widhopf et al and Queen et al comprises human framework regions, which as noted by Applicant above necessarily comprise amino acid residues at positions L1 and L2, and lack the amino acid insertion L39A present in chicken immunoglobulins. Thus, one of ordinary skill in the art following the motivation in the prior art as set forth above would have produced a method of making a humanized chicken immunoglobulin, wherein the humanized chicken immunoglobulin comprises CDRs from the donor chicken immunoglobulin and human acceptor framework regions, which necessarily comprise amino acid residues at positions L1 and L1 (Kabat numbering) and lack the amino acid insertion L39A (residue between amino acid positions L39 and L40; Kabat numbering) present in chicken immunoglobulin sequences. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979). See MPEP 2145.

With respect to the lack of a reasonable expectation of success, Applicant is reminded that objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results,

commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See, for example, *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). In the instant case, Andris-Widhopf et al teach partially humanized antibodies, "leaving only the variable regions for complete humanization at a later stage" (pg. 175, middle of 2nd col.), providing a reasonable expectation that a humanized chicken immunoglobulin could be established by one of ordinary skill in the art. Further, the humanization method of Queen uses framework regions from human variable domains having as little as 60% homology with the corresponding non-human variable region of the antibody to be humanized (e.g., see col. 13) and Queen applies the method to several different non-human antibodies that recognize different antigens (see Examples). Thus, the art recognized, that a variety of non-human antibodies could be humanized, even where there is low homology between the human and non-human variable region sequences. Applicant is reminded that obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).

For these reasons and those already of record, the rejection is maintained.

13. No claims are allowed.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

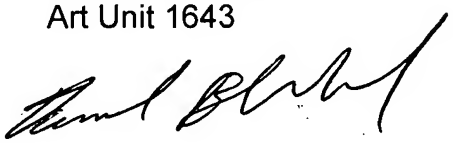
shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832.

The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Blanchard
Patent Examiner
Art Unit 1643



DB
April 10, 2007